Successful Erlotinib Rechallenge After Erlotinib-Induced Interstitial Lung Disease

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CASE REPORT

A 56-year-old nonsmoking Korean woman was diagnosed with stage 4 lung adenocarcinoma. Computed tomography (CT) scan showed a dominant left lung mass (Figure 1) with pulmonary, mediastinal, liver, adrenal, bone, and brain metastases. Erlotinib 150 mg daily and whole brain irradiation were started, and an epithelial growth factor receptor (EGFR) exon 19 mutation was detected. Symptoms improved until week 5 when she developed a new fever, worsening skin rash, and nonproductive cough. Erlotinib was held, and topical cleocin and oral doxycycline 200 mg daily were begun. Over the next 4 days, cough and dyspnea worsened with fall of O_2 saturation to 92%, prompting repeat CT scan. This revealed a tumor response; however, new extensive bilateral ground glass opacities consistent with erlotinib-induced interstitial lung disease (ILD) were noted (Figure 2). No further diagnostic studies were performed, and prednisone 60 mg daily was initiated. Fever, cough, and dyspnea improved 3 days later at which time she was placed on 40 mg daily. As she was not a candidate for current second-generation EGFR inhibitor trials, she was rechallenged with erlotinib 100 mg daily on day 10 (erlotinib stopped day 0). She remained afebrile with improved cough, dyspnea, and O_2 saturation on room air of 96%. The patient understood the risks, signed a new informed consent, and was given a peak flow meter for monitoring. On day 14, prednisone was decreased to 30 mg daily and doxycycline to 100 mg daily. On day 21, doxycycline was discontinued, and on day 28, prednisone was tapered to 20 mg daily. Erlotinib was increased to 150 mg on day 35 and prednisone tapered over next 3 weeks. Resolution of pneumonitis was confirmed by CT scan on day 60 (Figure 3) receiving full dose erlotinib off prednisone. Five months later, she had no further pulmonary complications.

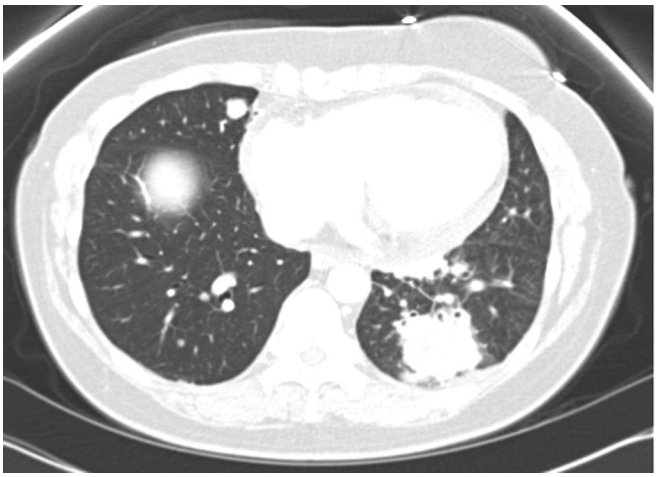

FIGURE 1. Initial CT showing dominant left lung mass with multiple pulmonary nodules. CT, computed tomography.

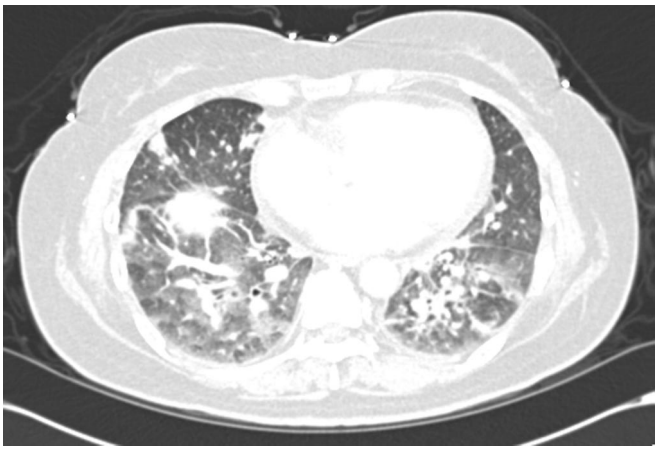

FIGURE 2. CT scan of a representative section of lung showing ground glass opacities consistent with erlotinib-induced ILD. CT, computed tomography; ILD, interstitial lung disease.

DISCUSSION

Erlotinib is recommended as first-line therapy for patients with EGFR-mutant lung cancer. ILD is a serious

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Disclosure: The authors declare no conflicts of interest.

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ISSN: 1556-0864/11/0606-1142

FIGURE 3. Improvement in both ILD and the primary lung mass. ILD, interstitial lung disease.

complication with an incidence estimated at 0.8%[1] and is fatal in approximately one third of cases. Permanent discontinuation of erlotinib is recommended along with the use of corticosteroids and supportive care. As this patient had a tumor response, we contacted pharmaceutical liaisons and confirmed there was little guidance on the safety of a rechallenge. In addition, clinical trials with second-generation EGFR inhibitors exclude patients with drug-associated ILD. There have been two recent reports describing treatment with erlotinib after gefitinib-induced ILD,[2–3] suggesting it may be possible to restart EGFR inhibitors in selected patients, especially those without a smoking history.[4] This is, to our knowledge, the first report of a successful erlotinib rechallenge after erlotinib-induced ILD. The prompt recognition of ILD allowed early discontinuation of erlotinib and institution of corticosteroids. We also hypothesize that the antiinflammatory properties of doxycycline[5] may have contributed to the rapid resolution of pulmonary symptoms; however, this would need to be confirmed in a prospective trial. We propose that patients with EGFR mutations who have been successfully treated for erlotinib-ILD and are receiving a dose of prednisone three-fourths 40 mg daily be considered for future kinase inhibitor treatments and clinical trials.

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